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EXPRESS MAIL CERTIFICATE

Date_____ Label No._____

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Name (Print) Signature

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Customer No.: **07278**

Docket No: 03394/100H557-US1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Ehud Goldin et al.

Serial No.: 09/851,494 Art Unit: 1646

Confirmation No.:

Filed: Examiner: John D. Ulm

For: **Gene Encoding A New TRP Channel Is Mutated In Mucolipodosis IV**

DECLARATION UNDER 37 C.F.R. § 1.131

Mail Stop Non-Fee Amendments
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Susan A. Slaugenhaupt, hereby declare and state as follows:

1. I am a citizen of the United States of America. I am more than twenty-one years of age.

2. I am a co-inventor of the above-identified application, along with James S. Acierno JR. James S. Acierno JR and I did the work that resulted in the data reported in the declaration, or it was done under my supervision as head of the laboratory.

3. I make this statement on behalf of myself and the co-inventors identified in paragraph 2.

4. I reaffirm my duty of candor and good faith in dealing with the Office, including the duty to disclose to the Office all information known to be material to the patentability of the invention as defined in 37 C.F.R. § 1.56.

5. I have read and am familiar with the instant application as it was filed in the U.S. Patent and Trademark Office.

6. I have read and am familiar with the publications by (i) Curtis et al. (Pub. No. US 2002/0035056 A1), which has an effective filing date under 35 U.S.C. 119(e) of Apr. 07, 2000; and (ii) Lal et al. (Pub. No. US 2002/0182671 A1), which has an effective filing date under 35 U.S.C. 119(e) of Aug. 17, 1999.

7. It is my understanding that, according to the Examiner, the amino acid sequence presented in SEQ ID NO: 3 of the instant application is identical to the amino acid sequence presented in SEQ ID NO: 2 of Curtis et al. and SEQ ID NO: 13 of Lal et al. It is further my understanding, that the Examiner states that Curtis et al. and Lal et al. each present an isolated nucleic acid encoding a protein comprising the amino acid sequence presented in

SEQ ID NO: 3 of the instant application, as well as a vector and host cell comprising that nucleic acid.

8. Prior to Aug. 17, 1999, the effective date of the Lal et al. publication, we conceived and reduced to practice the invention as described and claimed in claims 1, 5-7, and 33-34 of the subject application.

9. As evidence that our reduction to practice antedates Lal et al., we refer to Exhibits 1 and 2, which collectively establish the conception and reduction to practice of our invention prior to Aug 17, 1999. The exhibits document isolation and possession of a nucleic acid encoding MCOLN1 prior to Aug. 17, 1999. Dates, along with privileged information, appearing in these documents have been redacted, but each document has a date before August 17, 1999.

10. Exhibit 1 establishes identification of MCOLN1 sequence, showing the receipt by Dr. Slaugenhaupt of two primers: (i) sts-T66288-R (5'-AGC TGC AGG CCT ACA TCG -3'); and (ii) sts-T66288-F (5'GGC AGT CAG GTC GAA TCA AT-3). As shown in Appendix A, the two primers are specific to the MCOLN1 gene, spanning the 1732-1883 bp region of the MCOLN1 cDNA sequence (SEQ ID NO: 3).

11. Exhibit 2 documents identification and possession of a nucleic acid encoding a full-length MCOLN1 protein by showing an EST alignment spanning the MCOLN1 gene. At least two notations are particularly relevant. First, this page shows a "2264 bp"

annotation of T66288 following sequencing, indicating that T66288 encodes the entire MCOLN protein. Prior to our sequencing, the exact insert size of this construct was not known. Second, this page also identifies the orientation of AI8166064, which is the corresponding GenBank accession number for IMAGE CLONE 2517653 (Appendix B). Paragraph [0185] of the specification states that we "sequenced the IMAGE clone 2517653." This paragraph further describes our deduction and confirmation of the MG-2 (MCOLN) open-reading frame from this clone.

12. With the isolation and identification of the MCOLN1 coding region, we also achieved reduction to practice of an expression vector encoding the MCOLN1 protein prior to August 17, 1999. Appendix B reveals that IMAGE CLONE 2517653 (as presented in Exhibit 2) is inserted into the pBlusescript SK+ vector. This common vector is widely recognized by those skilled in the art of molecular biology as including T3 and T7 promoters that flank the cloning site, which allow expression of the inserted gene sequence. Appendix C shows the key structural features of this vector. The entire MCOLN1 open reading frame is present in IMAGE CLONE 2517653. Alternatively, given our identification of the coding sequence of MCOLN1, we knew how to incorporate that sequence into an expression vector such as pBluescript SK+.

13. These documents establish that the inventions of claims 1, 5-7, and 33-34 were reduced to practice prior to Aug. 17, 1999.

14. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true. I

further declare that these statements are made with the knowledge that the willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United Stated Code, and that such willful false statements may jeopardize the validity of the instant application or of any patent issued thereupon.

Respectfully submitted,

6/21/04
DATE

Susan A. Slaugenhaupt
Susan A. Slaugenhaupt

EXHIBIT A PAGE 1

IDT®

Integrated DNA Technologies, Inc.

1710 Commercial Park
Coralville, IA 52241
Phone: 800.328-2661
Fax: 319.626-8444
E-Mail: orders@idtdna.com
http://www.idtdna.com

Oligonucleotide Specification Sheet

Customer Information

Susan Slaugenhaupt
Harvard Institute of Human Genetics
Massachusetts General Hospital-Boston
77 Avenue Louis Pasteur HIM Bldg. Rm. 422
Boston, MA 02115
6174327025

Order Information

Order Date : [redacted]
Customer # : 19479
P.O. # : 0000085288

Sales order # : 148396
Reference #: 624757

Oligonucleotide Information

Reference # : **624757**
Purification : **Standard Purification**
Sequence Name : **sts-T66288-f**

Product : **DNA Oligo Sample**
Unit Size : **100 nmole**
Bases : **20**

Sequence : **5'- GGC AGT CAG GTC GAA TCA AT -3'**

10 × 4 = 40
10 × 2 = 20
60

Molecular Weight :	7,572.00
GC Content :	50.0 %
Tm (50mM NaCl) :	51.44 °C

Amount of Oligo

21.8	=	95.01	=	0.72
OD_{260}		nanomoles		mg

Printed 6/9/99

1569

LABELS - PEEL HERE

624757 Integrated DNA Tech
S. Slaugenhaupt 06/09/99
sts-T66288-f
5'-GGC AGT CAG GTC GAA TCA AT -3'
Tm = 51.44 °C, MW = 7572
21.80 OD_{260} = 95.01 nmol = 0.72 mg

624757 Integrated DNA Tech
S. Slaugenhaupt 06/09/99
sts-T66288-f
5'-GGC AGT CAG GTC GAA TCA AT -3'
Tm = 51.44 °C, MW = 7572
21.80 OD_{260} = 95.01 nmol = 0.72 mg

Samples Statistically Tested

Q.C. Approved By:

PLEASE READ BEFORE OPENING TUBES

* Store at -20°C. If the oligo is to be used on multiple occasions, resuspend in water or tris-EDTA buffer, divide into smaller aliquots, lyophilize, and store at -20°C.
* Contents may appear as either a translucent film or a white powder. This variance does not affect the quality of the oligo.
* Please centrifuge tubes prior to opening. Some of the product may have been dislodged during shipping.
* Calculations are made using 1 OD_{260} = 33 ug / mL

EXHIBIT A PAGE 2

IDT®

Integrated DNA Technologies, Inc.

Oligonucleotide Specification Sheet

1710 Commercial Park
Coralville, IA 52241
Phone: 800 328-2661
Fax: 319 626 8444
E-Mail: orders@idtdna.com
http://www.idtdna.com

Customer Information

Susan Slaugenhaupt
Harvard Institute of Human Genetics
Massachusetts General Hospital-Boston
77 Avenue Louis Pasteur HIM Bldg. Rm. 422
Boston, MA 02115
6174327025

Order Information

Order Date : [redacted]
Customer #: 19479
P.O. # : 0000085288

Sales order # : 148396
Reference #: 624758

Oligonucleotide Information

Reference # : **624758**
Purification : **Standard Purification**
Sequence Name : **sts-T66288-R**

Product : **DNA Oligo Sample**
Unit Size : **100 nmole**
Bases : **18**

Sequence : **5'- AGC TGC AGG GCT ACA TCG -3'**

11x4 = 44
7x2 = 14
58

Molecular Weight :	6,754.00
GC Content :	61.1 %
Tm (50mM NaCl) :	51.11 °C

Amount of Oligo				
15.5	=	75.73	=	0.51
OD_{260}		nanomoles		mg

Printed 6/9/99

1570

LABELS - PEEL HERE

624758 Integrated DNA Tech
S. Slaugenhaupt 06/09/99
sts-T66288-R
5'-AGC TGC AGG GCT ACA TCG -3'
Tm = 51.11 °C, MW = 6754
15.50 OD_{260} = 75.73 nmol = 0.51 mg

624758 Integrated DNA Tech
S. Slaugenhaupt 06/09/99
sts-T66288-R
5'-AGC TGC AGG GCT ACA TCG -3'
Tm = 51.11 °C, MW = 6754
15.50 OD_{260} = 75.73 nmol = 0.51 mg

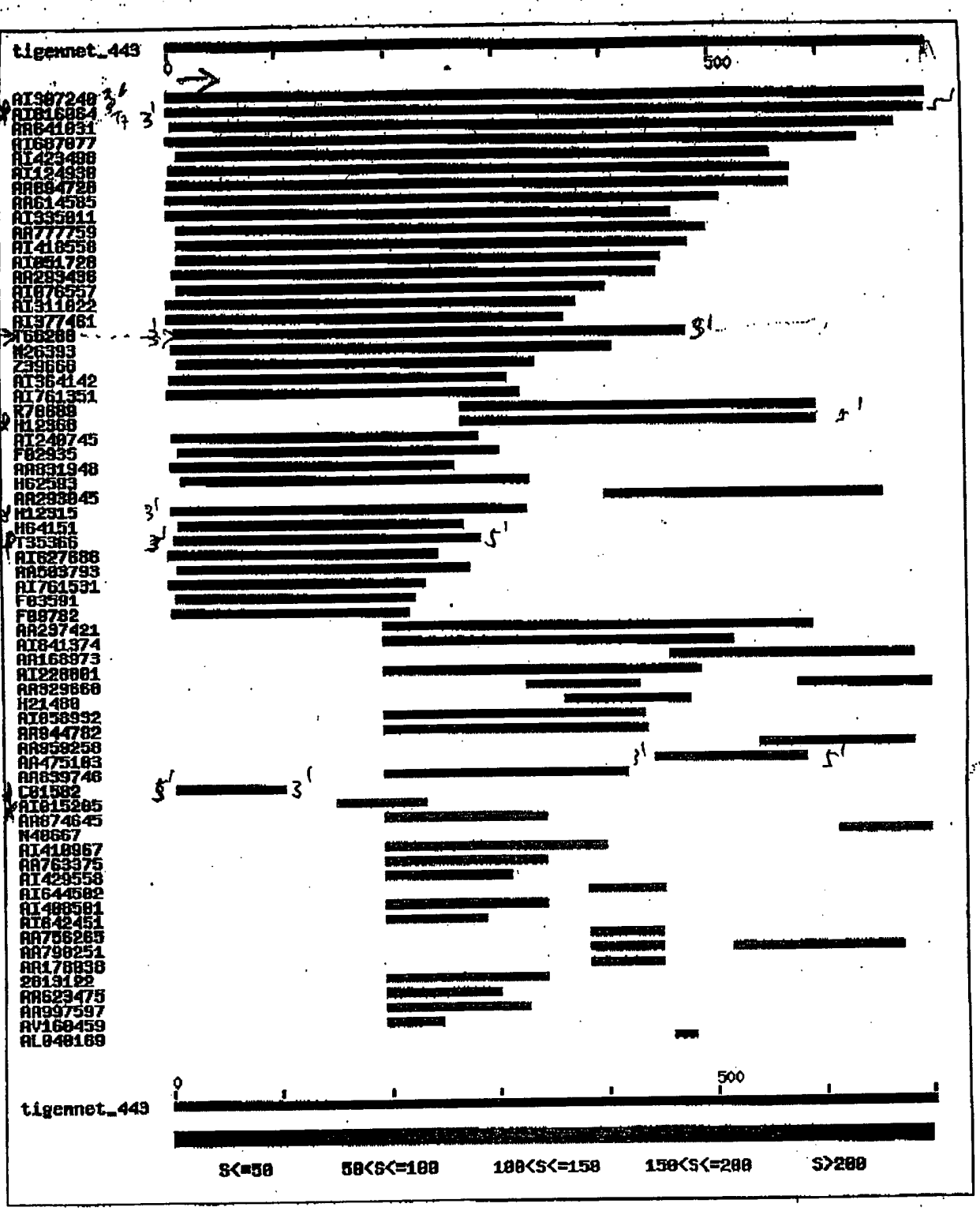
Samples Statistically Tested

Q.C. Approved By:

PLEASE READ BEFORE OPENING TUBES

- Store at -20°C. If the oligo is to be used on multiple occasions, resuspend in water or tris-EDTA buffer, divide into smaller aliquots, lyophilize, and store at -20°C.
- Contents may appear as either a translucent film or a white powder. This variance does not affect the quality of the oligo.
- Please centrifuge tubes prior to opening. Some of the product may have been dislodged during shipping.
- Calculations are made using 1 OD_{260} = 33 ug / mL

EXHIBIT B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SEQ ID NO: 2

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-------- **sts-T66288-r**

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```

APPENDIX B

The I.M.A.G.E. Consortium

"Sharing resources to achieve a common goal - the discovery of all genes "

Begin new search | Begin new Clone search

I.M.A.G.E. Clone Query Results:

Your search returned **2** results! Here they are:

Result Number	CLONE ID	ROW POS	COL POS	PLATE	GB ACCNUM	SEQ LENGTH	GB DATE CREATED	DATE MODIFIED	CDNA LIBR ID	SPECIES	TISSUE TYPE	VECTOR NAME
1	2517653	1	6	6268	AI815981	448	Jul 09 1999 12:00AM	Apr 17 2003 05:06PM	1341	human	brain/CNS	pBluescript SK+
2	2517653	1	6	6268	AI816064	706	Jul 09 1999 12:00AM	Apr 17 2003 05:06PM	1341	human	brain/CNS	pBluescript SK+

Begin new search | Begin new Clone search

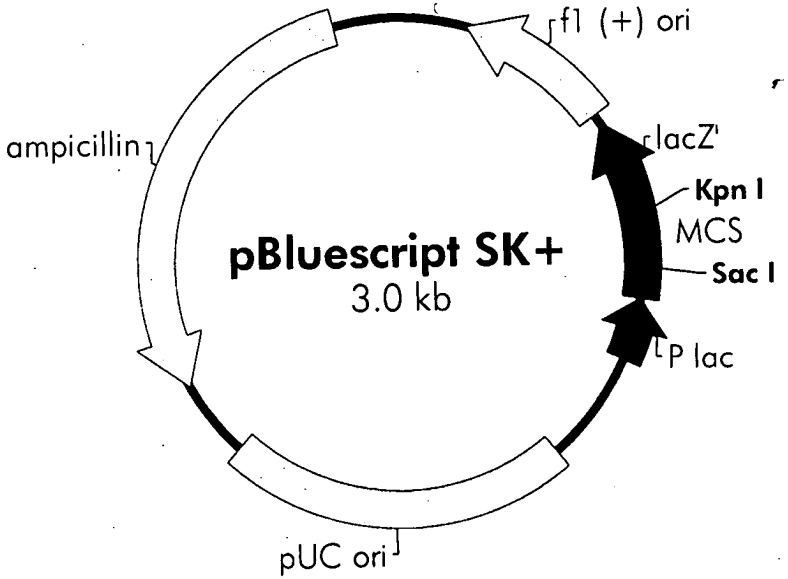
I.M.A.G.E. Consortium home page

BBRP home page

LLNL Programs, Projects, Centers and Consortia

APPENDIX C

f1 (+) origin 138–444
β-galactosidase α-fragment 463–816
multiple cloning site 653–760
***lac* promoter 817–938**
pUC origin 1158–1825
ampicillin resistance (*bla*) ORF 1976–2833



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